

REMARKS

Applicants enclose a Request for Continued Examination. Reconsideration and withdrawal of the rejections set forth in the Final Office Action dated March 2, 2004 are respectfully requested. Applicants petition for a one-month extension of time in which to file the response. A separate petition for the extension accompanies this paper.

I. Amendments

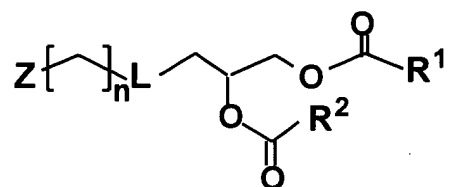
Claims 1 and 3 are amended to recite that L is selected from the group consisting of (i) -X-(C=O)-Y-, (ii) -X-(C=O)-, wherein X and Y are independently selected from oxygen, NH, and a direct bond, (iii) -O-CH₂-, and (iv) -CH₂-, effectively excluding the embodiment where L = NH-CH₂-.

II. Rejections under 35 U.S.C. §102

Claims 1-3, 5-15, and 28-33 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Wolff *et al.* (U.S. Patent No. 5,965,434).

A. The Invention

The present invention relates to a liposome composition, and to a method of delivering an agent with the liposomes, comprising a lipid having the formula:



wherein each of R¹ and R² is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms; n = 0-20; consisting of (i) -X-(C=O)-Y -, (ii) -X-(C=O)-, wherein X and Y are independently selected from oxygen, NH, and a direct bond, (iii) -O-CH₂-, and (iv) -CH₂-; and Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0.

B. The Cited Art

WOLFF ET AL. teach lipids of the general form A-B-C (Col. 5, line 5) where A is a hydrophobic moiety (e.g. a lipid), B is a spacer, and C is a cationic, pH-sensitive moiety. More specifically, and with respect to the spacer moiety B, Wolff *et al.* state:

"B is a spacer moiety *comprising* an alkane, alkene, ester, ether, glycerol, amide, heteroatom or a molecule that is cleaved under physiologic conditions" (Col. 5, lines 11-13).

Thus, in the general description of the lipid disclosed by Wolff *et al.*, B encompasses hundreds, possibly thousands, of moieties, due to the term "comprising". Wolff *et al.* provides working examples of the disclosed general lipid, and these specific examples are discussed more fully below.

C. Analysis

Wolff *et al.* disclose a general lipid of the form "A-B-C", discussed above, and also disclose specific examples. In this analysis section, the general "A-B-C" lipid is discussed, followed by a discussion of the specific examples.

1. Wolff *et al.*'s Lipid of the Form "A-B-C"

As noted above, the lipid of Wolff *et al.* is disclosed in its most broad terms as having the form "A-B-C", where the A, B, and C, moieties are defined in Wolff *et al.* on Col. 5, lines 8-17. Specifically, "A is a hydrophobic moiety *comprising*...; "B is a spacer moiety *comprising*...; and C is a cationic, hydrophilic, pH-sensitive moiety *comprising*...". Thus, each moiety A, B, and C, and therefore the lipid A-B-C, encompass a broad genus.

MPEP § 2131.02 states that "when the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated."

The CCPA has held that a broad genus does not anticipate a claimed species where one skilled in the art would have to choose judiciously from the dozens of

possibilities to arrive at the claimed species. *In re Kollman et al.*, 201 U.S.P.Q. 193 (C.C.P.A. 1979). *In re Ruschig*, 145 U.S.P.Q. 274 (C.C.P.A. 1965).

Set forth on ATTACHMENT 1 enclosed herewith is an analysis of the present structure and the A-B-C lipid of Wolff *et al.* As seen at the bottom of ATTACHMENT 1, for the purpose of analysis between the A-B-C lipid disclosed by Wolff *et al.* and the presently claimed lipid, the hydrophobic moiety "A" of Wolff *et al.* can be considered analogous to the R¹, R²-glycerol portion of the present structure and the "C" moiety of Wolff *et al.* analogous to the Z moiety of the present structure. Thus, a close inspection of spacer moiety "B" of Wolff *et al.* relative to the linker "L" of the present structure is required to determine if Wolff *et al.* anticipates.

ATTACHMENT 1 illustrates the various possible linking moieties "L" of the present structure. L can be eleven (11) groups, as set forth in blue ink in the table of ATTACHMENT 1. The moieties in black ink are duplicative of moieties in blue.

The class of substituents for the spacing moiety "B" in Wolff *et al.* is not well delineated, since the class is open ended due to the characterization by Wolff *et al.* of B being "a spacer moiety comprising....". This language leaves the selection of the linking or spacer moiety wide open, permitting the reader to select from the spacers listed by Wolff *et al.* or to select any other spacer not listed by Wolff *et al.* Moreover, as discussed in the next section, none of the specific embodiments disclosed by Wolff *et al.* show a lipid identical to the presently claimed structure, therefore it cannot be said that Wolff *et al.* provide guidance or state a preference for the claimed species. Thus, one of skill in the art, upon reading Wolff *et al.* would not be able to "at once envision" (M.P.E.P. § 2131.02) the compounds presently claimed.

Since "a broad genus does not anticipate a claimed species where one skilled in the art would have to choose judiciously from the dozens of possibilities to arrive at the claimed species" (*In re Kollman et al.*, 201 U.S.P.Q. 193 (C.C.P.A. 1979)), the present claims are not anticipated by the general, broad disclosure of an "A-B-C lipid" by Wolff *et al.*

2. Analysis of the Specific Examples Disclosed by Wolff *et al.*

As shown in ATTACHMENT 1, the present structure includes a moiety referred to as an R¹, R²-glycerol moiety, an "L" or linker moiety, and a "Z" moiety. As noted above, the

hydrophobic moiety "A" of Wolff *et al.* can be considered analogous to the R¹, R²-glycerol portion of the present structure and the "C" moiety of Wolff *et al.* analogous to the Z moiety of the present structure. Thus, a close inspection of spacer moiety "B" of Wolff *et al.* relative to the linker "L" of the present structure is required to determine if Wolff *et al.* anticipates.

Attached to this amendment is a copy of the portions of Wolff *et al.* with structures of specific embodiments, handmarked for analysis of the structures. Each specific example in Wolff *et al.* is marked to denote the R¹, R²-glycerol portion of the structure and the Z moiety. The L (i.e., "B") moieties are also indicated with a box.

As the Examiner can see, for the structures in Wolff *et al.* that include a R¹, R²-glycerol moiety, none of the spacer moieties ("L", "B") are identical to the linker groups claimed. Thus, none of the structures shown by Wolff *et al.* are identical to the structure presently claimed.

3. Conclusion

In summary, the broad generic disclosure of Wolff *et al.* of a lipid having the form "A-B-C" does not anticipate the present claims because the classes of substituents are sufficiently limited or well delineated to anticipate (M.P.E.P. § 2131.02) the present structure. None of the specific examples provided by Wolff *et al.* identically shows the presently claimed structure. Thus, Wolff *et al.* do not anticipate the present claims and withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

IV. Rejections under 35 U.S.C. §103

Claims 1-15 and 30-33 are rejected under 35 U.S.C. § 103(a) as allegedly upatentable over Wolff *et al.*

Claims 15 and 16 are rejected under 35 U.S.C. § 103(a) as allegedly upatentable over Wolff *et al.* further in view of Allen *et al.* (U.S. Patent No. 6,056,973).

Claims 17 and 18 are rejected under 35 U.S.C. § 103(a) as allegedly upatentable over Wolff *et al.* further in view of Zalipsky *et al.* (U.S. Patent No. 5,395,619).

A. The Invention

The invention has been described above.

B. The Prior Art

WOLFF ET AL. is discussed above.

ALLEN ET AL. teach a conjugate of the form "targeting ligand-polymer-lipid".

ZALIPSKY ET AL. describe a lipid-polymer conjugate where a lipid is attached to a hydrophilic polymer.

C. Analysis

According to the M.P.E.P. §2143.03: "To establish a prima facie case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art."

With respect to the rejection of claims 1-15 and 30-33 over Wolff *et al.*, Wolff *et al.* fail to show a lipid having the formula as claimed, as discussed above. There is simply no way to discern from the broad disclosure of Wolff *et al.* the specific lipids presently claimed. The broad genus of Wolff *et al.* is so broad that thousands of compounds are encompassed, and there is no guidance in the examples or specific embodiments for the lipid as presently claimed. Thus, the present claims are not obvious in view of Wolff *et al.* alone.

With respect to the rejection of claims 15 and 16, rejected over a combination of Wolff *et al.* in view of Allen *et al.*, and claims 17 and 18, rejected over a combination of Wolff *et al.* in view of Zalipsky *et al.*, these are patentable over the cited art because if an independent claim is nonobvious under 35 U.S.C. then any claim depending therefrom is nonobvious. (M.P.E.P. § 2143.03). Claims 15-18 are dependent, directly or indirectly, on claim 1, which defines over the cited primary reference to Wolff *et al.* for the reason given above. The secondary references, Allen *et al.* and Zalipsky *et al.* cited for teachings of ligands and polymer chains, do not disclose the missing information from Wolff *et al.* to show all of the present claim limitations. Accordingly, withdrawal of the rejections under 35 U.S.C. § 103 is respectfully requested.

V. Conclusion

In view of the foregoing, the applicant submits that the claims pending patentably define over the cited art. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4402.

Respectfully submitted,

Date: June 8, 2004

Judy M. L.
Judy M. Mohr
Registration No. 38,563

Correspondence Address:

Customer Number 27777
ALZA Corporation
C/o Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933